UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,958	09/28/2005	Jens Pohl	2923-725	1440

6449 7590 09/26/2007

ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
KEMMERER, ELIZABETH	

ART UNIT	PAPER NUMBER
1646	

NOTIFICATION DATE	DELIVERY MODE
09/26/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/550,958	POHL ET AL.	
	Examiner	Art Unit	
	Elizabeth C. Kemmerer, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,18,22,24-27* is/are rejected.

7)☒ Claim(s) *17,19-21 and 23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of species MP52 in the reply filed on 02 July 2007 is acknowledged. However, upon further consideration, the requirement to elect a species is *withdrawn* and all species will be examined.

Status of Application, Amendments, And/Or Claims

The preliminary amendment of 28 September 2005 has been entered. Claims 1-27 are under examination.

Claim Objections

Claim 4 is objected to because of the following informalities: there appear to be two typographical errors in claim 4. First, "TGF-f3" appears t be an error wherein "TGF-β" was intended. Second, "activinor" appears to be a typographical error wherein "activin or" was intended. Appropriate correction is required.

Claims 17, 19, 20, 21, and 23 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

35 U.S.C. §§ 101 and 112, Second Paragraph – "Use of" Claims

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-27 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). For the purposes of this office action, claims 24-27 are being interpreted as being directed to methods of treating a subject comprising administering the recited osteoinductive material to a subject.

Claims 24-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claims 24-27 provide for the use of an osteoinductive material, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Furthermore, claim 24 specifies that the morphogenetic proteins have been proven to be "useful." It is not clear in what context the proteins must be useful. For example, almost all proteins are arguably useful as

nutritional supplements, or as molecular weight markers. However, the claim does not specify the manner in which the recited proteins must be useful.

35 U.S.C. § 112, First Paragraph – Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure enables one skilled in the art to make and use the claimed invention in its full scope without resorting to undue experimentation include: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples; (4) the nature or complexity of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims. See *In re Wands*, 8 USPQ2d. 1400 (Fed. Cir. 1988).

Regarding the nature of the invention, as stated above, claims 24-27 are being interpreted as being broadly directed to methods of treating a subject comprising administering the recited osteoinductive material to a subject. Furthermore, claim 25

specifically recites preventing various symptoms or conditions, and claims 25-27 recite diverse symptoms, conditions, and/or target tissues. Such is highly complex, as it involves physiological responses to complex biological molecules. The courts have acknowledged this subject matter as being unpredictable. As was found in Ex parte Hitzeman, 9 USPQ2d 1821 (BPAI 1987), a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. See also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991).

The state of the art shows that many members of the TGF-β superfamily of proteins have activity on diverse tissues. Such is reviewed in the instant specification. However, the claims are directed to administering an *osteoinductive* material comprising osteoinductive proteins and a matrix. There is no guidance in the specification or the prior art as to how to administer such compositions, which have been shown to specifically grow bone, in order to treat tissues other than bone (such as neural tissue, liver, kidney, cardiovascular tissue, pancreas, renal tissue, uterine tissue, mucous membranes, endothelium, epithelium, and tissue of the sensory system. A great deal of experimentation would have been required of the skilled artisan to determine how to use a material designed to grow bone in tissues other than bone or the related tissues of

cartilage, connective tissue (e.g., tendon, ligament), periodontal tissue, and dental tissue.

Furthermore, "prevention" has been used in the art to mean total protection from a future event. While the art has shown that osteoinductive compositions comprising an osteoinductive protein and a matrix can be used to *treat* bone defects, it has not shown that bone defects can be *prevented.*

Due to the large quantity of experimentation necessary to determine how to use the recited osteoinductive compositions to treat tissues that are unrelated to bone or to prevent any symptom or condition, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, the contradictory state of the prior art as reviewed in the instant specification, the unpredictability of the effects of complex biological molecules on physiological systems, and the breadth of the claims which recite diverse symptoms/conditions and further recite "prevention", undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 8, 11-16, 18, 22, and 24-27 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0567391A1 (Bristol-Myers Squibb Company; published 27 October 1993).

EP 0567391A1 teaches osteoinductive material comprising a matrix material (demineralized bone matrix, DBM) and, adsorbed on inner and/or outer surfaces of this matrix material, morphogenetic proteins (TGF-β_1), wherein the material was obtained by combining the matrix and the protein using a buffer at pH 2.5, which kept the protein stable and allowed for even coating. See col. 8, Example 1. This is relevant to claim 1. It is noted that TGF-β_1 inherently contains a 7 cysteine region as per claim 2, is at least a variant as per claim 3, belongs to the TGF-β family as per claim 4, is inherently a dimeric protein as per claim 5, and inherently has a sequence fitting one of the formulas of claim 8. DBM is a biocompatible material as per claim 11, is "natural" as per claim 12, and is porous as per claim 13. Example 1 further provides a process for making the material as recited in claim 22.

EP 0567391A1 further teaches addition of polylactide derivatives as per claim 14. See col. 5 second paragraph.

EP 0567391A1 further teaches a buffer for coating having an ionic concentration of 30mM as required by claim 15. See col. 8, Example 1.

EP 0567391A1 further teaches the buffer further comprising saccharides (mannitol) as required by claim 16, and soaps (Tween-80^{TM}) as required by claim 18. See col. 9, first paragraph.

Finally, EP 0567391A1 teaches a method of using the material to treat bone defects as recited in claims 24-27. See col. 6, starting at line 34.

35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6, 7, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0567391A1 as applied to claims 1-5, 8, 11-16, 18, 22, and 24-27 above, and further in view of EP 1074620A1 (HyGene AG, published 07 February 2001).

As discussed above, EP 0567391A1 teaches osteoinductive material comprising a matrix material (demineralized bone matrix, DBM) and, adsorbed on inner and/or outer surfaces of this matrix material, morphogenetic proteins (TGF-β_1), wherein the material was obtained by combining the matrix and the protein using a buffer at pH 2.5, which kept the protein stable and allowed for even coating.

EP 0567391A1 does not teach the proteins specified in claims 6, 7, 9, and 10, such as a monomeric form of MP52.

However, EP 1074620A1 teaches a monomeric form of MP52 meeting the limitations of claims 6, 7, 9, and 10, and that it has similar properties to other TGF-β proteins, since it is a member of that family. See p. 5, paragraphs [0021] to [0022].

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the osteoinductive material of EP 0567391A1 by using the monomeric MP52 of EP 1074620A1 with a reasonable expectation of success. motivation to combine the references can be found in EP 1074620A1, who teach that the protein is useful in combination with a matrix (p. 7, paragraph [0038] and who also teach that the monomeric MP52 is stable (p. 3, paragraph [0009].

Thus, the invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

Claims 17, 19, 20, 21, and 23 are objected to. Claims 1-16, 18, 22, and 24-27 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (571) 272-0874. The examiner can normally be reached on Monday through Thursday, 7:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D. can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ECK

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646